AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method to detect a nucleotide or nucleoside, comprising:

[[a)]] separating a purine or pyrimidine base from a ribose or deoxyribose moiety of the nucleotide or nucleoside;

[[b)]] depositing the separated purine base or pyrimidine base on a surface enhanced Raman spectroscopy (SERS) substrate;

synthesizing a double-strand molecule comprising the separated purine base or pyrimidine base and a single strand target molecule on the SERS substrate; and

[[c)]] detecting the separated purine or pyrimidine base using SERS.

2. (Original) The method of claim 1, wherein the method detects a deoxynucleotide triphosphate.

3. (Original) The method of claim 2, wherein the method further comprises including the deoxynucleotide triphosphate in a nucleic acid sequencing reaction mixture before separating the purine or pyrimidine base from the purine or pyrimidine moiety.

4. (Original) The method of claim 1, wherein the purine or pyrimidine base is associated with a Raman label before it is detected by SERS.

5. (Original) The method of claim 1, wherein the nucleotide or nucleoside comprises a purine base.

6. (Original) The method of claim 5, wherein the base consists essentially of adenine.

7. (Original) The method of claim 5, wherein the base consists essentially of guanine.

8. (Original) The method of claim 1, wherein the surface enhanced Raman spectroscopy is surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS).

9. (Original) The method of claim 8, wherein the nucleotide or nucleoside comprises a pyrimidine base.

10. (Original) The method of claim 9, wherein the nucleotide or nucleoside comprises thymine.

11. (Original) The method of claim 9, wherein the nucleotide or nucleoside comprises uracil.

12. (Original) The method of claim 9, wherein the nucleotide or nucleoside comprises cytosine.

13. (Currently amended) The method of claim 1, wherein the single strand target molecule is deposited on silver nanoparticles.

14. (Original) The method of claim 13, wherein the target molecule is contacted with an alkali-metal halide salt.

15. (Original) The method of claim 14, wherein the alkali-metal halide salt is lithium chloride.

16. (Currently amended) A method to detect a single strand target molecule comprising a purine base or a pyrimidine base, comprising:

[[a)]] ~~isolating~~ obtaining the single strand target molecule;

[[b)]] depositing the single strand target molecule on a surface enhanced Raman spectroscopy (SERS) substrate;

synthesizing a double-strand molecule comprising a complimentary purine base or pyrimidine base and the single strand target molecule on the SERS substrate; and

[[c)]] detecting Raman scattering from the ~~irradiated target~~ double-strand molecule using surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS) ~~, thereby detecting~~ to detect a sequence of the single strand target molecule.

17. (Currently amended) The method of claim 16, wherein the single strand target molecule is isolated from a biological sample.

18. (Currently amended) The method of claim 16, wherein the single strand target molecule is a nucleotide, a nucleoside, or a base.

19. (Currently amended) The method of claim 18, wherein the single strand target molecule consists essentially of a pyrimidine base.

20. (Original) The method of claim 19, wherein the base consists essentially of thymine.

21. (Original) The method of claim 19, wherein the base consists essentially of uracil.

22. (Original) The method of claim 19, wherein the base consists essentially of a cytidine.

23. (Currently amended) The method of claim 16, wherein the single strand target molecule is a nucleotide triphosphate.

24. (Currently amended) A method to detect ~~identical~~ nucleotides at consecutive ~~target~~ positions ~~in a~~ complimentary to a single strand template nucleic acid molecule, comprising:

[[a)]] contacting ~~a known number of copies of~~ the single strand template nucleic acid molecule with a reaction mixture comprising a primer, a polymerase, and a known initial

concentration of a first nucleotide to form a post-reaction mixture, the primer or the template single strand nucleic acid being immobilized on a surface of the reaction chamber, ~~wherein the 3' terminus of the primer binds to the nucleic acid molecule upstream of a 5' nucleotide of the consecutive target positions~~;

synthesizing a double-strand molecule comprising the first nucleotide and the single strand template nucleic acid;

[[b)]] depositing the post-reaction mixture on a surface enhanced Raman spectroscopy (SERS) substrate;

[[c)]] detecting a concentration of the first nucleotide using SERS; and

[[d)]] determining whether ~~more than~~ one or more of the first nucleotide was ~~added to the consecutive target positions~~ synthesized to the single strand template nucleic acid.

25. (Currently amended) The method of claim 24, wherein the known number of copies of the single strand template nucleic acid molecule is about the same as a known number of first nucleotide molecules in the reaction mixture.

26. (Currently amended) The method of claim 24, wherein the known number of copies of the single strand template nucleic acid molecule is about one half a known number of first nucleotide molecules in the reaction mixture.

27. (Currently amended) The method of claim 24, further comprising adding additional first nucleotide to the reaction mixture after said detecting the concentration of the first nucleotide.

28. (Original) The method of claim 24, further comprising cleaving a base from the nucleotide and detecting the base using SERS.

29. (Currently amended) The method of claim 24, wherein the detecting the concentration of the first nucleotide using SERS ~~detection~~ is surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS).

30. (Currently amended) The method of claim 24, further comprising repeating said steps [[a-d]] of claim 24 with a different nucleotide.

31. (Original) The method of claim 24, wherein the nucleotide is attached to a Raman label before it is detected by SERS.

32. (Original) The method of claim 24, wherein an internal control is included in the reaction mixture and detected using SERS.

33. (Currently amended) The method of claim 32, wherein the SERS signal of the internal control and the nucleotide is compared to determine whether more than one nucleotide was added to the consecutive ~~target~~ positions complimentary to the single strand template nucleic acid molecule.

34. (Currently amended) A method to determine a nucleotide occurrence at a target position of a single strand template nucleic acid molecule, comprising:

[[a)]] contacting a detectable number of the single strand template nucleic acids with a reaction mixture in a reaction chamber, the reaction mixture comprising a primer, a polymerase, and an initial concentration of a first nucleotide ~~triphosphate~~, the primer or the single strand template nucleic acid being immobilized on a surface of the reaction chamber;

[[b)]] incubating the reaction mixture to allow binding of the primer to the single strand template nucleic acid and formation of a post-reaction mixture;

synthesizing a double-strand molecule comprising the first nucleotide and the single strand template nucleic acid;

[[c)]] depositing the post reaction mixture, or a component thereof, on a surface enhanced Raman spectroscopy (SERS) substrate; and

[[d)]] detecting a Raman signal from the first nucleotide using SERS, wherein a decrease in intensity of the Raman signal of the first nucleotide in the post-reaction mixture identifies an extension reaction product, thereby identifying the nucleotide occurrence at the target position.

35. (Currently amended) The method of claim 34, further comprising repeating the steps [[a-d]] of claim 34 with a different nucleotide until the nucleotide occurrence is identified.

36. (Currently amended) The method of claim 35, further comprising washing the SERS substrate ~~before optionally repeating steps a-d~~.

37. (Original) The method of claim 34, wherein the incubation time is about 1 second to 10 minutes.

38. (Original) The method of claim 34, wherein the reaction chamber is less than 100 nm in at least one dimension.

39. (Currently amended) The method of claim 34, wherein a pre-reaction SERS analysis is performed on the first nucleotide before it contacts the single strand template nucleic acid molecule.

40. (Original) The method of claim 39, wherein a decrease in intensity of the SERS signal of the first nucleotide in the post-reaction mixture compared to the pre-reaction mixture identifies the extension reaction product.

41. (Currently amended) The method of claim 34, wherein the method is performed twice for the target ~~nucleotide~~ position, using dATP and dGTP one at a time as the first nucleotide and a second nucleotide.

42. (Original) The method of claim 41, wherein the complementary strand of the template nucleic acid molecule is immobilized in a second reaction chamber and the method is performed an additional two times, again using dATP and dGTP one at a time as the first nucleotide and the second nucleotide.

43. (Original) The method of claim 34, wherein an internal control is included in the reaction mixture and detected using SERS.

44. (Original) The method of claim 43, wherein the SERS signal of the internal control and the nucleotide is compared to identify the nucleotide occurrence at the target position.

45. (New) The method of claim 1, wherein the detecting is by monitoring a differential concentration of the separated purine base or pyrimidine base before and after the synthesizing of the double-strand molecule.

46. (New) The method of claim 16, wherein the detecting is by monitoring a differential concentration of a purine base or pyrimidine base before and after the synthesizing of the double-strand molecule.

47. (New) The method of claim 24, wherein the detecting is by monitoring a differential concentration of a purine base or pyrimidine base before and after the synthesizing of the double-strand molecule.

48. (New) The method of claim 34, wherein the detecting is by monitoring a differential concentration of a purine base or pyrimidine base before and after the synthesizing of the double-strand molecule.